Safety of new multidrug-resistant TB drugs: results from the end TB observational study

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Background

Multidrug-resistant tuberculosis (MDR-TB) requires long treatment using a combination of drugs known to cause adverse events. Injectable drugs may cause hearing loss, renal failure and electrolyte depletion; linezolid may cause peripheral neuropathy and myelosuppression. Bedaquiline and delamanid, the first new TB drugs registered in 40 years, as well as other commonly used drugs, may cause QT interval prolongation, a risk factor for sudden death. We aimed to assess the safety of MDR-TB regimens containing bedaquiline or delamanid.

Methods

This is a multi-centre prospective observational study of patients who received bedaquiline or delamanid as part of a MDR-TB regimen from April 2015 until June 2017 in 15 countries. Safety data collection included reporting of a predefined set of nine adverse events (AE) of special interest irrespective of severity. Clinically relevant adverse events were defined as an AE of special interest reported at a severity grade considered to be clinically relevant, either because it should lead to a change in TB regimen, or because it required supplementation.

Results

In total, 1244 patients were included. The most common clinically relevant AEs of special interest were electrolyte depletion (26%), peripheral neuropathy (24%) and hearing loss (17%). The least common were myelosuppression (4%), acute renal failure (4%), QT interval prolongation (3%) and optic neuritis (2 %). Overall, AEs commonly associated with injectables or linezolid were frequent: 35.6% of 643 patients who received an injectable from the start experienced at least one of hearing loss, acute renal failure, or electrolyte depletion, 11.0% of 1020 patients who received linezolid from the start, experienced at least one peripheral neuropathy, optic neuritis or myelosuppression. In contrast, QT interval prolongation was experienced by 2.7% of patients who received bedaquiline (848) or delamanid (354) or both (42) from the start.

Conclusions

Bedaquiline and delamanid are safe and QT interval prolongation is infrequent. However, AEs frequently associated with the other drugs in MDRTB regimens are common. Close monitoring and management of AEs in patients treated for MDR-TB is required.

Bedaquiline and delamanid are safe but adverse events associated to other drugs in MDRTB regimens are common. Close monitoring and management of adverse events in patients treated for MDR-TB is important.